

Supporting Information

High Affinity Rigidified AT₂ Receptor Ligands with Indane Scaffolds

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Content of Supplementary data:

- 1. Chiral GC–MS chromatograms of compounds 15a/b and 16a/b.**
- 2. HPLC purity of test compounds**
- 3. Computational details**
- 4. References**

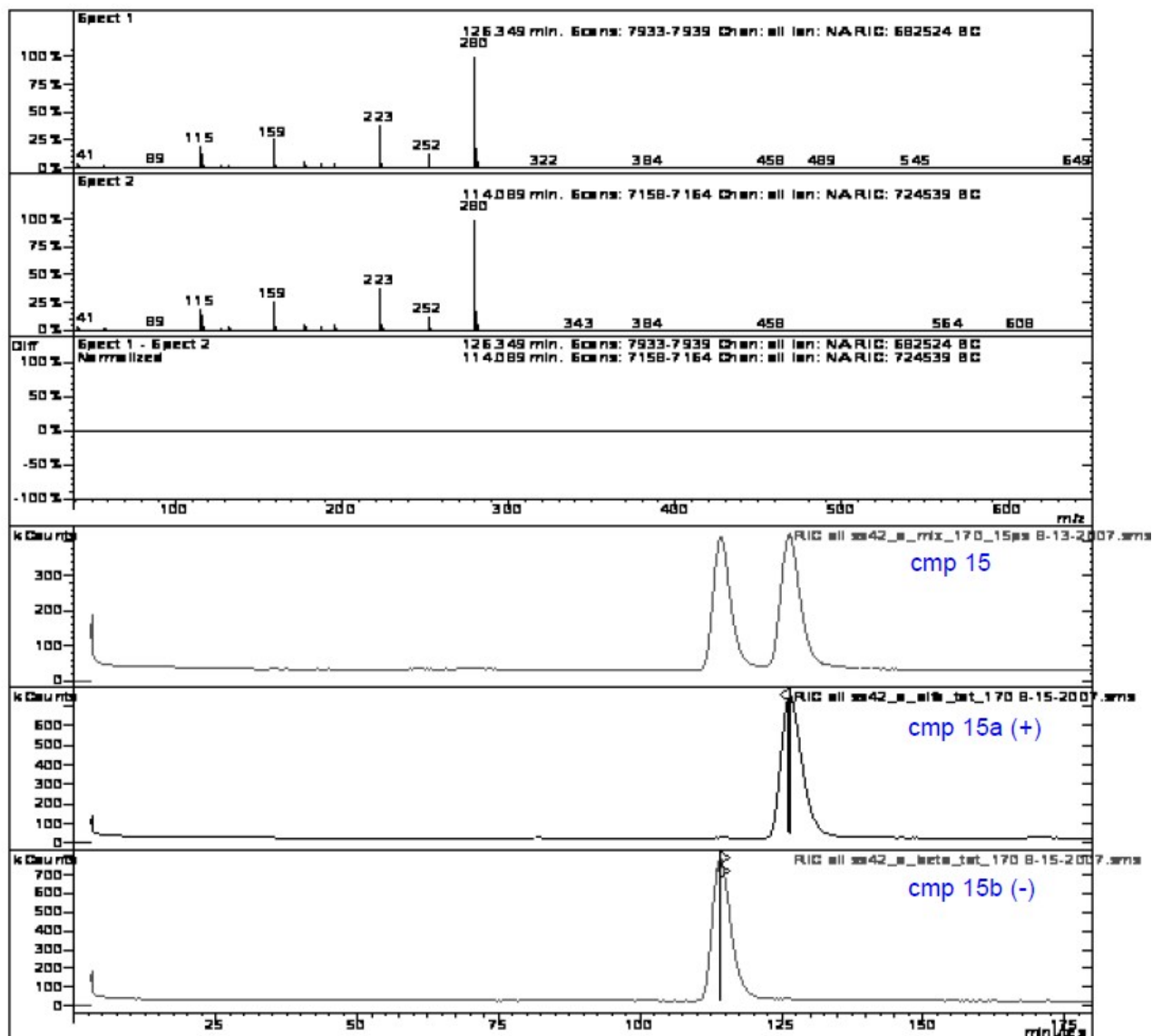
1. Chiral GC-MS chromatograms of compounds 15a/b and 16a/b.

The isolated enantiomers **15a** and **15b** are compared to the racemic mixture of **15**. The isolated enantiomers **16a** and **16b** are compared to a mixture of **16a**:**16b** of approximately 1:5.

15a and **15b**: GC-MS, m/z : 280 ($M - CH_3$); 252; 223; 159; 115.

Chromatogram Plots

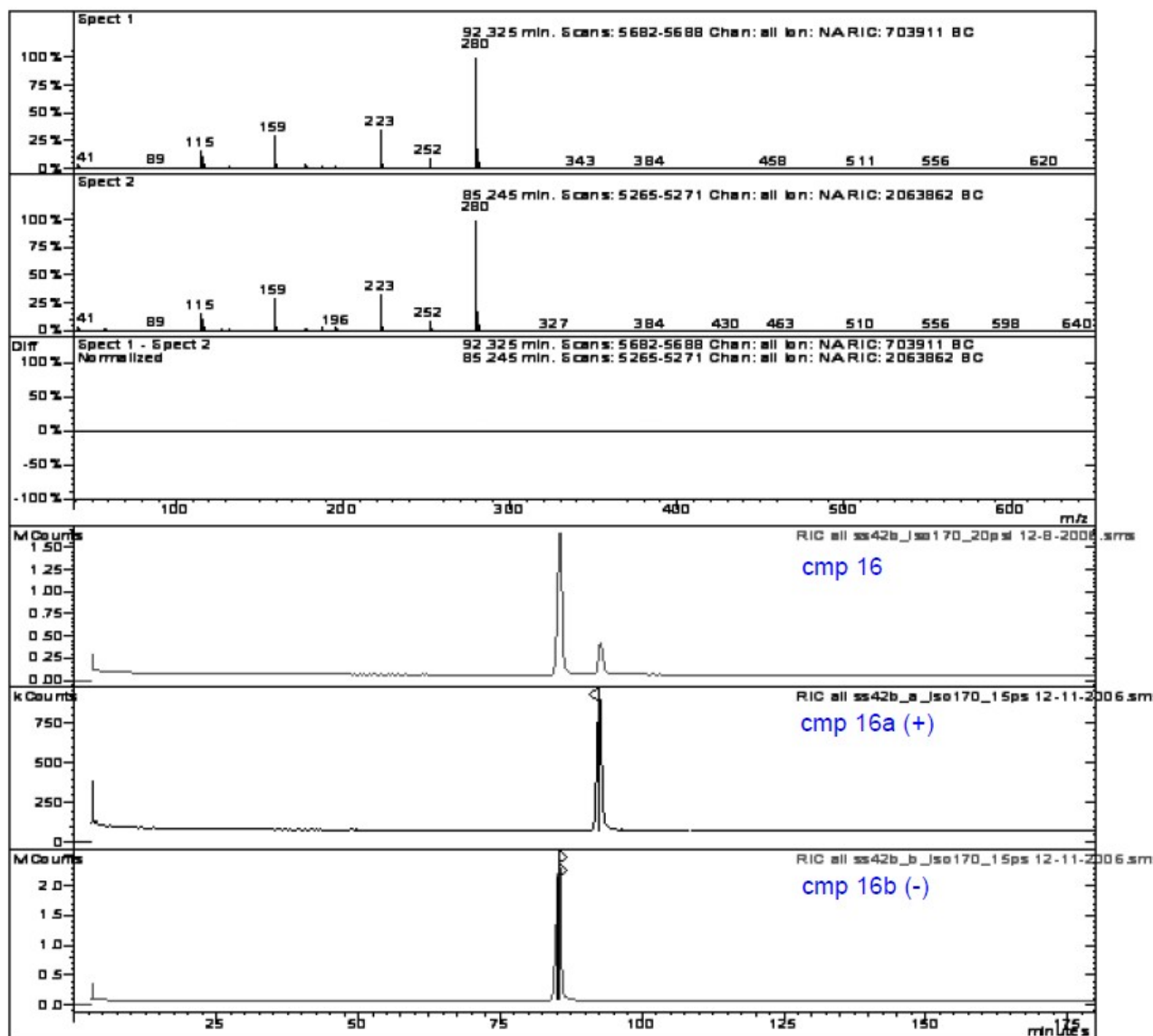
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16a and 16b: GC-MS, m/z : 280 ($M - CH_3$); 252; 223; 159; 115.

Chromatogram Plots

Plot 1: c:\... \ss42b_iso170_20ps1 12-8-2006.sms RIC all
Plot 2: c:\... \ss42b_a_iso170_15ps 12-11-2006.sms RIC all
Plot 3: c:\... \ss42b_b_iso170_15ps 12-11-2006.sms RIC all



2. HPLC purity of test compounds

Table 1. Purity of test compounds determined by two different HPLC systems.

	C4^a		C18^b	
	Retention time (min)	Purity (%)	Retention time (min)	Purity (%)
7a	11.22	99.8	10.12	100
7b	11.38	99.7	10.12	100
8a	11.35	99.5	10.12	100
8b	11.33	100	10.10	99.1
9a	11.65	100	10.48	100
9b	11.53	100	10.47	99.8
10a	11.65	99.8	10.41	100
10b	11.62	100	10.41	100

a) Column: Thermo HyPurity C4, 5 μ m (4.6x50 mm). Buffer A: 0.1% TFA in water. Buffer B: 0.09% TFA in MeCN. Flow rate: 1.5 ml/min. Gradient: 10-50% B in 15 min. Detection: UV at 220 nm. b) Column: ACE C18, 5 μ m (4.6x50 mm). Buffer A: 0.1% TFA in water. Buffer B: 0.09% TFA in MeCN. Flow rate: 1.5 ml/min. Gradient: 20-60% B in 15 min. Detection: UV at 220 nm.

3. Computational details

Model structures were built of the compounds by replacing the *n*-butyl chain connected to the sulfoncarbamate with a methyl group. Conformational analysis was performed in MacroModel¹ using the OPLS 2005 force field and the Generalized Born solvent accessible (GB/SA) surface area method for water.² The conformational analysis was performed using the Systematic unbound multiple minimum³ search method, with 1000 search steps per investigated torsion angle. For minimization Truncated Newton conjugate gradient was used with a maximum of 500 iterations and convergence criterion set to 0.05 kJ mol⁻¹ Å⁻¹. Unique conformations, based on a maximum atom deviation cutoff of 0.5 Å, within 21 kJ mol⁻¹ of the lowest energy minimum were saved in the conformational search.

A common spatial arrangement of structural moieties (excluding the isopropyl substituents), was identified between the lowest and second lowest energy conformations found for the enantiomer pairs, with $\Delta E = 0.077$ kJ mol⁻¹ and 0.335 kJ mol⁻¹ for **7a/b** and **10a/b** model structures, respectively. These conformations of each enantiomer pair were superimposed using all atoms.

4. References

1. MacroModel, version 10.6, Schrödinger, LLC, New York, NY, 2014.
2. Still, W. C.; Tempczyk, A.; Hawley, R. C.; Hendrickson, T. Semianalytical Treatment of Solvation for Molecular Mechanics and Dynamics. *J. Am. Chem. Soc.* **1990**, *112*, 6127-9.
3. Goodman, J. M.; Still, W. C. An unbounded systematic search of conformational space. *J. Comput. Chem.* **1991**, *12*, 1110-17.